In re: Application of TERADA et al.

Serial No.: 10/045,721

Page 2 of 9

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

- (Currently Amended) A method for identifying a drug candidate for promoting tissue-specific differentiation of [[a]] an embryonic stem cell (ES), the method comprising the steps of:
 - (A) providing a library of test substances, the library comprising at least a first test substance and a second test substance, the first and second test substances having different molecular structures;
 - (B) providing an *in vitro* culture of undifferentiated embryonic stem cells (ES), the culture being divided into at least a first subculture and a second subculture and;
 - (C) culturing the first and second subcultures for at least about [[3]] 5 days in the absence of a test substance;
 - (D) contacting the first subculture with a first test substance and the a second subculture with [[the]] a second test substance;
 - (E) culturing the first and second subcultures between for 7 to 18 days wherein an early stage differentiation test substance is added on days 9 to 12, a mid stage differentiation test substance is added from day 12 to 18; and
 - (F) analyzing the cells in the first and second subcultures for increased tissuespecific gene expression.
- 2. (Cancel).
- 3. (Previously presented) The method of claim 1, wherein the embryonic stem cells are mammalian embryonic stems cells.

{WP299669;1}

In re: Application of TERADA et al.

Serial No.: 10/045,721

Page 3 of 9

- 4. (Cancel)
- 5. (Currently Amended) The method of claim 1, wherein the murine embryonic stem cells are murine R1 embryonic stem cells.
- 6. (Currently Amended) The method of claim 1, wherein the mammalian embryonic stem cells are human embryonic stem cells.
 - 7. (Cancelled)
 - 8. (Currently amended) The method of claim 1, wherein the conditions that would promote tissue specific differentiation of the stem colls comprises culturing the first and second subcultures comprising the first and second test substances are cultured at about 37°C in a humidified, carbon-dioxide containing incubator.

Claims 9-13. (Cancelled).

- 14. (Previously Presented) The method of claim 1, wherein the step (F) of analyzing the cells in the first and second subcultures for increased tissue-specific gene expression comprises isolating mRNA from the first and second subcultures.
- 15. (Original) The method of claim 14, wherein total cellular RNA is isolated from the first and second subcultures.
- 16. (Previously Presented) The method of claim 14, wherein the step (F) further comprises reverse-transcribing the mRNA to create cDNA.
- 17. (Previously Presented) The method of claim 1, wherein the step (F) of analyzing the cells in the first and second subcultures for increased tissue-specific gene expression comprises performing a polymerase chain reaction (PCR).

In re: Application of TERADA et al.

Serial No.: 10/045,721

Page 4 of 9

- 18. (Original) The method of claim 14, wherein the isolated mRNA is immobilized on a substrate.
- 19. (Original) The method of claim 18, wherein the substrate is contacted with a probe that specifically hybridizes to the tissue-specific mRNA.
- 20. (Previously Presented) The method of claim 1, wherein the step (F) of analyzing the cells in the first and second subcultures for increased tissue-specific gene expression is performed using gene chip technology.